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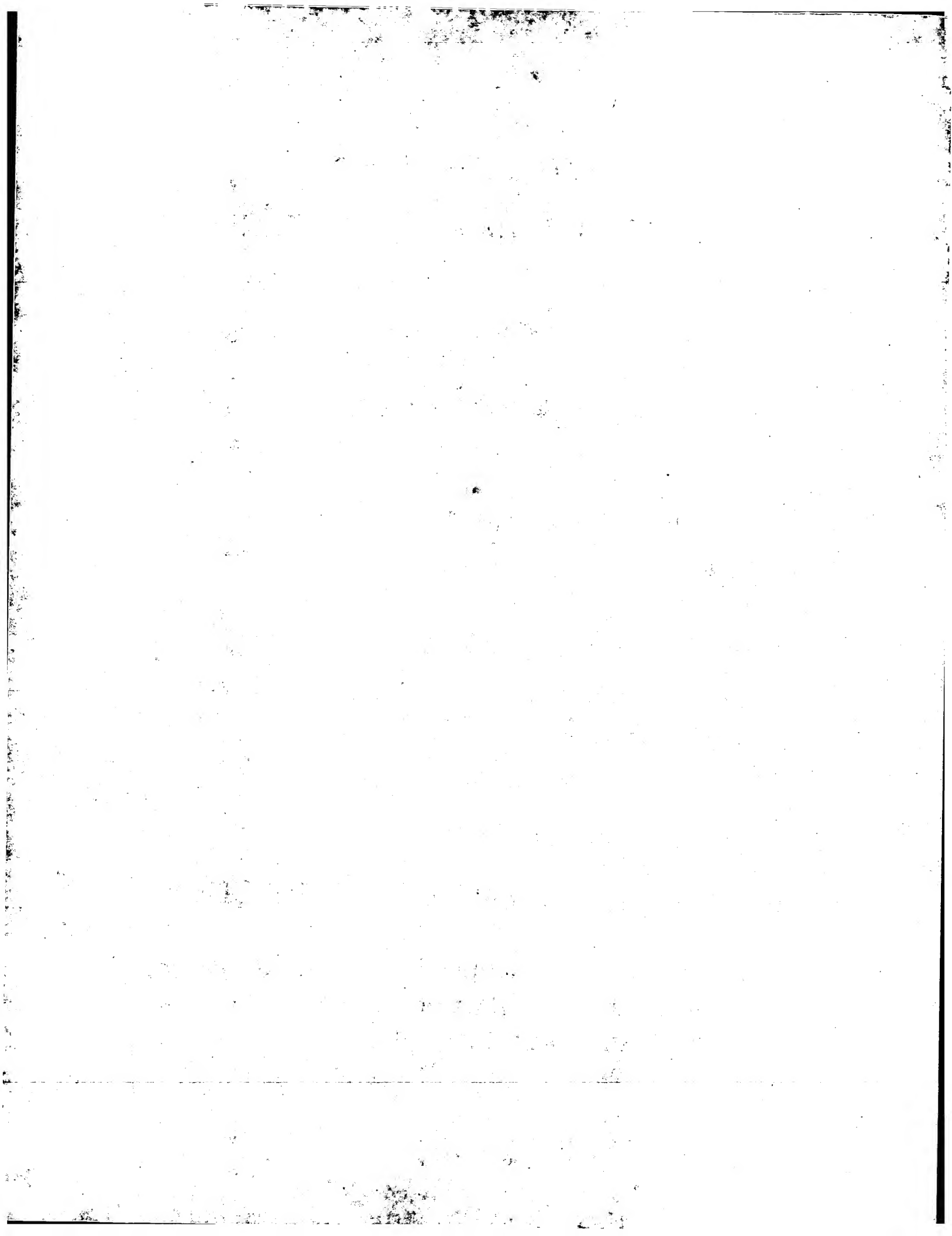
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- (21) International Application Number: PCT/US02/05724 (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.
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- (71) Applicant (*for all designated States except US*): MERCK & CO., INC. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US).
- (72) Inventors; and  
(75) Inventors/Applicants (*for US only*): UJJAINWALLA, Feroze [GB/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). CHU, Lin [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). GOULET, Mark, T. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). LEE, Bonnie [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). WARNER, Daniel [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). WYVRATT, Matthew, J. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US).
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(54) Title: ACYLATED PIPERIDINE DERIVATIVES AS MELANOCORTIN-4 RECEPTOR AGONISTS

(57) Abstract: Certain novel 4-substituted N-acylated piperidine derivatives are agonists of the human melanocortin receptor(s) and, in particular, are selective agonists of the human melanocortin-4 receptor (MC-4R). They are therefore useful for the treatment, control, or prevention of diseases and disorders responsive to the activation of MC-4R, such as obesity, diabetes, sexual dysfunction, including erectile dysfunction and female sexual dysfunction.



WO 02/068388 A3

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US02/05724

<b>A. CLASSIFICATION OF SUBJECT MATTER</b>		
IPC(7) :IPC7 A61K 31/445, 31/505; C07D 401/06, 401/14, 451/09 US CL :Please See Extra Sheet According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b>		
Minimum documentation searched (classification system followed by classification symbols) U.S. : 514/256, 316, 318, 326; 544/335; 546/124, 187, 193; 548/953		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) CAS-structure EAST/WEST-subclass, melanocortin		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 6,166,037 A (BUDHU et al.) 26 December 2000, see entire document, especially column 75-76 formula XXXIII and XXXIX.	1-15, 21, 28
Y	Database CAPLUS on STN (Columbus, OH, USA) No. 133:159566, 'MC3-R as a novel target for antiinflammatory therapy' Abstract, Getting et al. 2000, vol.13, No.1, pages 19-27, see entire document.	16-28
Y	Database CAPLUS on STN (Columbus, OH, USA) No. 108:150205, 'Highly regioselective synthesis of trisubstituted pyrrolidines by 1,2-cycloaddition' Chem. Phar. bull. 1987, vol. 35, no. 7, pages 2646-55, see compounds with RN attached.	1-15
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.		
* Special categories of cited documents:	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention	
"A" document defining the general state of the art which is not considered to be of particular relevance	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone	
"E" earlier document published on or after the international filing date	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art	
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"G" document member of the same patent family	
"O" document referring to an oral disclosure, use, exhibition or other means		
"P" document published prior to the international filing date but later than the priority date claimed		
Date of the actual completion of the international search 05 SEPTEMBER 2002	Date of mailing of the international search report 10 DEC 2002	
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-9230	Authorized officer CELIA CHANG Telephone No. (703) 308-1235	

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/05724

## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X, P	Database CAPLUS on STN (Columbus, OH, USA) No. 135:166844, 'Preparation of piperazinyl and piperidinyl ketones useful for treating or prevention neuronal damage and for stimulating nerve growth'. Tomlinson et al, August 2001, see compounds of RN attached.	1-15, 21, 28

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US02/05724

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
  
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☒ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
  
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.  
☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/05724

## A. CLASSIFICATION OF SUBJECT MATTER:

US CL :

514/256, 316, 318, 326; 544/335; 546/124, 187, 193; 548/959

## BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING

This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claims 1-10, 16-21 in part (r=1, s=1 or r=2, s=0), 11-15 and 28, drawn to piperidinyl pyrrolidinyl compounds composition and method of use.

Group II, claims 1-10, 16-21 in part (r=2, s=1, r=1, s=2), drawn to piperidinyl piperidines, composition and method of use.

Group III, claims 1-10, 16-21 in part (r=2, s=2), drawn to azepidinyl compounds, composition and method of use.

Group IV, claims 1-10, 16-21 in part (r=1, s=0), drawn to four membered ring nitrogen containing compounds, composition and method of use.

Group V, claims 22, 26-27, drawn to composition and method of treating diabetes or obesity.

Group VI, claims 23-25, drawn to composition and method of treating erectile dysfunction.

The inventions listed as Groups I-VI do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the compounds of groups I-IV have distinct structure and at least one of the Markush alternatives is not novel (see CA 130:223167RN 221142-59-2 anticipated group I). Groups V-VI are drawn to combination of active ingredients for treating disease which are not dependent on the novelty of the compounds for patentability. Under Rule 13.2 Annex B Markush Practice part I, paragraph (f)(i)(B)(1)v when dealing with alternatives, if it can be shown that at least one Markush alternative is not novel over the prior art, the question of unity of invention shall be reconsidered by the examiner.

